

REMARKS

Formal Matters

In the Specification:

The specification is amended to correct recitation of Figures 1A and 1B.

The specification is also amended to correct trademark designations of TAQMAN<sup>®</sup> PCR.

The title is amended to more particularly describe the claimed subject matter.

The first paragraph of the specification is amended to update and correct inadvertent errors in claiming priority.

In the Claims:

Claims 1, 3, and 24-35 are pending in the application.

Claims 1, 25, 27-30, 33 and 35 are amended merely to more particularly point out and claim the subject matter of the invention. The amendment to recite “high stringency conditions” is supported throughout the specification, such as at page 8, line 26 to page 9, line 7; and page 52, lines 23-24. The amendment to recite detecting the level of expression of a nucleic acid sequence is found throughout the specification such as at, for example, page 14, lines 26-28; page 27, lines 35-36; page 38, line 28 to page 39, line 3; and page 50, lines 22-23. The term “marker gene” or “marker probe” is amended to “marker sequence” merely to provide consistent antecedent basis for the term. Support for the amendment is found in claims 28 and 33 and in the descriptions of marker probe provided in the context of Fig. 2 and the legend for Fig.2. Claim 30 is amended with respect to marker SHGC-36123 merely to correct an inadvertent typographical error. Support for the amendment to SHGC-361232 is found in Table 6, page 47 and in the legend to Table 6 on page 47. Marker EST00087 is deleted from claim 30 because it represents more than one sequence. Claims 27 and 35 are amended merely to correct an inadvertent typographical error.

No new matter is added by the amendments.

Objections to the Specification

Brief Description of the Drawings - Figures 1A and 1B: The description for Figures 1A and 1B were objected to as lacking separate descriptions. The figure legend for Figures 1A and 1B has been amended to provide separate descriptions. References to Figures 1A and 1B have been corrected in the specification.

Use of the term "Taqman" in the specification: Recitations of Taqman have been corrected throughout the specification to recite "TAQMAN<sup>®</sup> PCR."

The title: The title is objected to as not being descriptive. The title is amended to recite Methods of Diagnosing Tumor in a Mammal.

Claims to priority: The first paragraph of the specification listing the claims of priority has been amended to correct inadvertent errors.

The objections to the specification have been overcome by the above amendments. Withdrawal of the objections is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 3, and 24-35 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because the phrase "under stringent conditions" is allegedly unclear. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The phrase "stringent conditions" is defined in the specification as synonymous with the phrase "high stringency conditions" which is further described in the paragraphs at page 8, line 26 to page 9, line 7, particularly in the paragraph at page 8, line 35 to page 9, line 7. Thus, the full set of conditions encompassed by the claims is clear and withdrawal of the rejection is respectfully requested.

Claim 30 is rejected under Section 112, second paragraph, as being indefinite because the exact meaning of the phrase "Stanford Human Genome Center Marker Probes SHCG-1235, ..." is allegedly unclear as to whether the phrase is a trademark. Applicants respectfully traverse the rejection, and point out that the phrase refers to a publicly available DNA marker probe. Further description of the SHGC markers is provided below. The marker designation is not a trademark and does not require

capitalization or generic terminology for the purpose of protecting the mark. Withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 3, and 24-35 are rejected under 35 U.S.C. § 112, first paragraph as claiming subject matter that allegedly is not described in the specification. According to the Examiner, claims to a method of detecting a gene or genes encoding a CT-1 polypeptide are allegedly not described in the specification because the structural elements of a gene that would encode the DNA sequences, promoter and regulatory sequences and defining elements of a “gene” are not disclosed in the specification (Office Action Paper No. 8 at pages 4 and 5). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims.

The term “gene” was also used by Applicants in the specification to refer to the coding sequence of CT-1 (see, for example, page 21, lines 8-9). One of ordinary skill in the art would readily understand that detection of gene expression refers to expression of the coding sequence. Without acquiescing to the rejection and merely to advance prosecution, Applicants amended the claims to recite a method of diagnosing tumor by detecting an increase in the level of expression of a nucleic acid sequence in a test sample relative to expression of the nucleic acid sequence in a control sample, where the detecting is by contacting the nucleic acid sequence with a probe comprising at least 20 contiguous nucleic acid bases from SEQ ID NO:1 or SEQ ID NO:2 (DNA encoding CT-1 polypeptide). Detection of the expression level of a nucleic acid sequence is disclosed throughout the specification, such as at page 14, lines 26-28; page 27, lines 35-36, page 38, line 28 to page 39, line 3; and page 50, lines 22-23. As a result, the claimed subject matter is encompassed by the specification. Withdrawal of the rejection is respectfully requested.

Claim 28 claims a method of detecting the number of copies of a nucleic acid sequence in a test sample relative to a marker sequence on the chromosome encoding the nucleic acid sequence in the test sample, which marker sequence is not amplified. Applicants disclose chromosome mapping of an amplified nucleic acid sequence, such as SEQ ID NO:1, in the specification (see, for example, page 22, lines 19-26; and page 43,

line 3 to page 49, line 25). Guided by this disclosure coupled with ordinary knowledge of the relevant literature, one of ordinary skill in the art can readily determine the chromosome and chromosome location of a nucleic acid sequence probed according to the invention. Thus, claim 28 encompasses subject matter disclosed by the specification.

Based on the above discussion regarding, the rejection of claims 1, 3, and 24-35 have been overcome and withdrawal of the rejection is respectfully requested.

Claims 1, 3, and 24-35 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that allegedly is not described in the specification, specifically referring to the a probe comprising at least 20 nucleotides of SEQ ID NO:1. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Applicants disclose hybridization methods using nucleic acid probes comprising at least 20 nucleic acid bases at page 14, lines 33-34. As a result, the claims encompass subject matter disclosed in the specification. Withdrawal of the rejection is respectfully requested.

Claims 29-30 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that allegedly is not described in the specification, specifically requesting the location of support for the phrase in claim 29, “a nucleic acid sequence comprising at least 20 contiguous nucleic acid bases from a sequence, or its complement, in Chromosome 16 from chromosomal regions selected from the group consisting of regions P7, P55, P89, P90, P92, P93, P94, P95, P99, P154, and P208.” Support for the phrase is found in the specification at, for example page 14, lines 33-34 (regarding a nucleic acid sequence probed of at least 20 nucleic acid bases); page 44 (Table 3 listing Chromosome 16 map positions P7, P55, P99, P154, and P208); and page 47 (Table 6 listing Chromosome 16 map positions P89, P90, P92, P93, P94, and P95). Thus, claims 29-30 contain subject matter disclosed in the specification. Withdrawal of the rejection is respectfully requested.

Claim 30 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter allegedly not described in the specification in such a way as to enable one skilled in the art to practice the invention, specifically concerning the public availability of the marker sequences encompassed by the claim. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The rejection is in two parts: First if the marker sequence designations recited in claim 30 are trademarks, the invention cannot be practiced. Second, if the marker sequence designations are not trademarks, then evidence of the public availability of the marker sequences is required.

Applicants pointed out, *supra*, that the marker sequence designations are not trademarks. Marker EST00087 is deleted from claim 30 because the designation represents multiple sequences. Evidence of the public availability of the marker sequences as designated is provided in the following table:

Marker Sequence Designation	NCBI/GenBank Accession Number
SHGC-2835	G17883
SHGC-9643	G11276
SHGC-11302	G14518
SHGC-2726	G17879
SHGC-36123	G30069
SHGC-35326	G28577
IB391	T03509
GATA7B02	G07935
SHGC-33727	G28154
SHGC-13574	G14802

On the above-listed NCBI/GenBank accession numbers were listed as being synonymous with the listed SHGC marker number. The rejection of claim 30 is, thus, overcome and withdrawal of the rejection is respectfully requested.

Based on the above comments, all of the rejections under Section 112, first paragraph have been overcome. Withdrawal of the rejections and allowance of the claims is respectfully requested.

### SUMMARY

The title is amended to reflect the claimed subject matter. The specification is amended to correct inadvertent typographical errors and other informalities.

Claims 1, 3, and 24-35 are pending in the application. Claims 1, 3, 27-30, 33, and 35 are amended merely to more particularly point out the subject matter of the invention or to correct an inadvertent spelling error.

No new matter is added to the title, specification, or claims by the amendments.

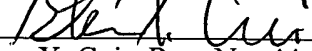
The claim rejections under section 112 first and second paragraphs are overcome by the discussions provided herein. Withdrawal of the rejections is respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is strongly encouraged to call the undersigned at the number indicated below.

This response/amendment is timely submitted with a transmittal letter, petition, and fees for a three-month extension of time. In the unlikely event that this document is separated from the transmittal letter, applicants petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Respectfully submitted,  
GENENTECH, INC.

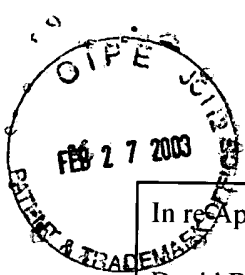
Date: February 27, 2003

By:   
Steven X. Cui - Reg. No. 44,637  
for Deirdre L. Conley - Reg. No. 36,487  
Telephone No. (650) 225-2066



09157

PATENT TRADEMARK OFFICE



02-28-03

Patent Docket P2533C2

cup 1647

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of David Botstein et al.  Serial No.: 09/723,703  Filed: November 28, 2000  For: METHODS OF DIAGNOSING TUMOR IN A MAMMAL (AS AMENDED)	Group Art Unit: 1642  Examiner: L. Helms  EXPRESS MAIL LABEL NO.: <u>EV 016 019 305</u> <u>US</u>  DATE OF DEPOSIT: <u>FEBRUARY 27, 2003</u>
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AMENDMENT TRANSMITTAL

Assistant Commissioner of Patents  
Washington, D.C. 20231

Sir:

Transmitted herewith is an amendment in the above-identified application.

The fee has been calculated as shown below.

	Claims Remaining After Amendment		Highest No. Previously Paid For	Present Extra	Rate	Additional Fees
Total	14	-	20	0	18	\$0.00
Independent	2	-	3	0	84	\$0.00
___ 0 Multiple dependent claim(s), if any					280	\$0.00
Total Fee Calculation						\$0.00

      X        
                    
      X      

No additional fee is required.

The Commissioner is hereby authorized to charge Deposit Account No. 07-0630 in the amount of \$. **A duplicate copy of this transmittal is enclosed.**  
Petition for Extension of Time is enclosed.

The Commissioner is hereby authorized to charge any additional fees required under 37 CFR 1.16 and 1.17, or credit overpayment to Deposit Account No. 07-0630. **A duplicate copy of this sheet is enclosed.**

Respectfully submitted,  
GENENTECH, INC.

Date: February 27, 2003

By: Steven X. Cui  
Steven X. Cui - Reg. No. 44,637  
for Deirdre L. Conley - Reg. No. 36,487  
Telephone No. (650) 225-2066



09157

PATENT TRADEMARK OFFICE

**VERSION WITH MARKINGS TO SHOW CHANGES MADE****In the Title:**

The title has been amended as follows, wherein strikeout in brackets [00] indicates deleted terminology and underling 00 indicates added terminology.

~~[CARDIOTROPHIN-1 COMPOSITIONS AND METHODS FOR THE TREATMENT OF TUMOR]~~METHODS OF DIAGNOSING TUMOR IN A MAMMAL

**In the Specification**

The specification has been amended as follows, wherein strikeout in brackets [00] indicates deleted terminology and underling 00 indicates added terminology.

Please replace the paragraph beginning at page 1, line 7, with the following rewritten paragraph:

This is a continuation application claiming priority to U.S. application Serial Number 09/648,183, filed August 25, 2000, issued October 29, 2002 as U.S. Patent No. 6,472,585, which is a continuation of U.S. Application Serial No. 09/234,730, filed January 21, 1999, which is a [non-provisional] continuation-in-part application of U.S. Application Serial No. 09/033,114, filed March 2, 1998, which is a continuation of U.S. Application Serial No. 08/733,850, filed October 18, 1996, now abandoned, which is a continuation of U.S. Application Serial No. 08/443,129 filed May 17, 1995, issued May 6, 1997 as U.S. Patent No. 5,627,073, which is a divisional of U.S. Application Serial No. 08/286,304 filed August 5, 1994, issued November 5, 1996 as U.S. Patent No. 5,571,893, which is a continuation-in-part of U.S. Application Serial No. 08/233,609 filed April 25, 1994, issued July 9, 1996 as U.S. Patent No. 5,534,615, and to U.S. Provisional Application Serial No. 60/113,296, filed December 22, 1998, the entire disclosure of which is hereby incorporated by reference.

Please replace the paragraph beginning at page 4, line 23, with the following rewritten paragraph:

~~[Figure]~~Figures 1A and 1B (SEQ ID NO: 1 and 2) ~~[shows]~~show the nucleotide sequence of DNA58125 beginning in Figure 1A and continuing onto Figure 1B. DNA58125~~[that]~~ is a cDNA encoding a native sequence cardiotrophin-1 (CT-1). SEQ ID NO:1 is the coding strand of DNA58125 and SEQ ID NO:2 is the complementary strand of DNA58125. SEQ ID NO:3, shown in Figure 1A, is the derived amino acid sequence of a native sequence cardiotrophin-1 (CT-1).

Please replace the paragraph beginning at page 7, line 32, with the following rewritten paragraph:

As used herein, the terms a "CT-1" polypeptide is used to refer to a polypeptide comprising a native sequence polypeptide having the same amino acid sequence as a corresponding CT-1 polypeptide derived from nature, and fragments of such native sequence polypeptides. Such native sequence CT-1 polypeptides can be isolated from nature or, along with the respective fragments, can be produced by recombinant and/or synthetic means. The term specifically encompasses naturally-occurring truncated or secreted forms (*e.g.*, an extracellular domain sequence), naturally-occurring variant forms (*e.g.*, alternatively spliced forms) and naturally-occurring allelic variants of the CT-1 polypeptide. In one embodiment of the invention, the native sequence CT-1 is a full-length native presequence or a mature form of a CT-1 polypeptide shown in Figure 1A (SEQ ID NO:3). Fragments of the respective native polypeptides herein include, but are not limited to, polypeptide variants from which the native N-terminal signal sequence has been fully or partially deleted or replaced by another sequence, and extracellular domains of the respective native sequences, regardless whether such truncated (secreted) forms occur in nature.

Please replace the paragraph beginning at page 52, line 20, with the following rewritten paragraph:

DNA comprising the coding sequence of full-length or mature CT-1 (as shown in ~~[Figure 1, SEQ ID NO:1 and 2]~~Figures 1A and 1B, SEQ ID NOs:1 and 2) is employed as

a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of CT-1) in human tissue cDNA libraries or human tissue genomic libraries.

Please replace the paragraph beginning at page 21, line 10, with the following rewritten paragraph:

According to the present invention, such genes have been identified by quantitative PCR (S. Gelmini *et al.*, Clin. Chem. 43, 752 [1997]), by comparing DNA from a variety of primary tumors, including breast, lung, colon, prostate, brain, liver, kidney, pancreas, spleen, thymus, testis, ovary, uterus, etc. tumor, or tumor cell lines, with pooled DNA from healthy donors. Quantitative PCR was performed using a [TaqMan] TAQMAN<sup>®</sup> PCR instrument (ABI). Gene-specific primers and fluorogenic probes were designed based upon the coding sequences of the DNAs.

Please replace the paragraph beginning at page 38, line 16, with the following rewritten paragraph:

The starting material for the screen was genomic DNA isolated from a variety of cancers. The DNA is quantitated precisely, *e.g.* fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, [TaqMan<sup>™</sup>] TAQMAN<sup>®</sup> PCR) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System<sup>™</sup> (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding CT-1 is over-represented in any of the primary lung or colon cancers or cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 1. An explanation of the abbreviations used for the designation of the primary tumors listed in Table 1 and the primary tumors and cell lines referred to throughout this example has been given hereinbefore. The results of the [TaqMan<sup>™</sup>] TAQMAN<sup>®</sup> PCR are reported in delta ( $\Delta$ ) Ct units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so

on. Quantitation was obtained using primers and a [TaqMan<sup>TM</sup>]TAQMAN<sup>®</sup> PCR fluorescent probe derived from the CT-1-encoding gene. Regions of CT-1 which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are preferred for the primer and probe derivation, *e.g.* a 3'-untranslated region. The sequences for the primers and probes (forward, reverse and probe) used for the CT-1 gene amplification were as follows:

CT-1 (DNA58125):

58125.tm.fl

5'-TTCCCAGCCTCTCTTTGCTTT-3' (SEQ ID NO: 4)

58125.tm.r1

5'-TCAGACGGAGTTACCATGCAGA-3' (SEQ ID NO: 5)

58125.tm.p1

5'-TGCCCCGTTCTCTTA ACTCTTGGACCC-3' (SEQ ID NO: 6)

Please replace the paragraph beginning at page 43, line 18 with the following rewritten paragraph:

The fluorometrically determined concentration was then used to dilute each sample to 10 ng/μl in ddH<sub>2</sub>O. This was done simultaneously on all template samples for a single [TaqMan<sup>TM</sup>]TAQMAN<sup>®</sup> PCR plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with [TaqMan<sup>TM</sup>]TAQMAN<sup>®</sup> PCR primers and probe both B-actin and GAPDH on a single plate with normal human DNA and no-template controls. The diluted samples were used provided that the Ct value of normal human DNA subtracted from test DNA was  $\pm 1$  Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough for 8-9 plates or 64 tests.

Please replace the paragraph beginning at page 47, line 5 with the following rewritten paragraph:

Table 6 describes the epicenter markers that were employed in association with CT-1 (DNA58125). These markers are located in close proximity to DNA58125 and are used

to assess the amplification status of the region of chromosome 16 in which DNA58125 is located. The distance between individual markers is measured in centirays, which is a radiation breakage unit approximately equal to a 1% chance of a breakage between two markers. One cR is very roughly equivalent to 20 kilobases. The marker SHGC-36123 is the marker found to be the closest to the location on chromosome 16 where DNA58125 most closely maps. However, the [~~TaqMan~~<sup>TM</sup>]TAQMAN<sup>®</sup> PCR primers and probes for SHGC-2726 failed in our assay due to technical difficulties related to PCR.

In the Claims:

Claims 1, 25, 27-30, 33, and 35 are amended as follows, wherein strikeout in brackets [00] indicates deleted terminology and underling 00 indicates added terminology.

1. (Twice Amended) A method of diagnosing tumor in a mammal, the method comprising:

(a) detecting the level of expression of a [~~gene encoding a cardiotrophin-1 (CT-1) polypeptide~~] nucleic acid sequence in a test sample of tissue cells obtained from the mammal, wherein the cells are suspected of uncontrolled growth and wherein the detecting is by contacting, under [~~stringent~~]high stringency conditions, nucleic acid of the test sample cells with a nucleic acid probe comprising at least 20 contiguous nucleic acid bases from DNA 58125 (SEQ ID NO:1) or its complement (SEQ ID NO:2);

(b) detecting, as in step (a) the level of expression of [~~a gene encoding a cardiotrophin-1 (CT-1) polypeptide~~] the nucleic acid sequence in a control sample of tissue cells of the same cell type that do not exhibit uncontrolled growth; and

(c) comparing the [~~CT-1~~] expression level of the nucleic acid sequence in the test cells with the expression level in the control cells, wherein a higher expression level in the test sample indicates the presence of tumor in the mammal.

25. (Amended) The method of claim 1 wherein the [CT-1] expression level of the nucleic acid sequence in the test sample cells is at least two-fold greater than in the control cells.
27. (Amended) The method of claim 26 wherein the cancerous tissue is selected from the group consisting of breast cancer, prostate cancer, colon cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colorectal cancer, endometrial [~~cancer~~carcinoma], salivary gland carcinoma, kidney cancer, vulval cancer, thyroid cancer, and head and neck carcinoma.
28. (Amended) A method of diagnosing tumor in a mammal, the method comprising:
- (a) detecting the number of copies of a [~~gene encoding a cardiotrophin-1 (CT-1) polypeptide~~]nucleic acid sequence in a test sample of tissue cells obtained from the mammal, wherein the cells are suspected of uncontrolled growth and wherein the detecting is by contacting, under [~~stringent~~]high stringency conditions, nucleic acid of the test sample cells with a nucleic acid probe comprising at least 20 contiguous nucleic acid bases from DNA 58125 (SEQ ID NO:1) or its complement (SEQ ID NO:2);
  - (b) detecting the number of copies of a nucleic acid marker sequence on the chromosome encoding [~~a cardiotrophin-1 (CT-1) polypeptide~~]the nucleic acid sequence in the test sample, which marker gene is not amplified; and
  - (c) comparing the [~~CT-1 gene~~] copy number of the nucleic acid sequence in the test cells with the [~~gene~~] copy number of the marker [~~gene~~]sequence, wherein a higher [~~CT-1 gene~~]nucleic acid sequence copy number indicates the presence of tumor in the mammal.
29. (Amended) The method of claim 28 wherein the marker sequence is detected by contacting, under [~~stringent~~]high stringency conditions, nucleic acid of the test sample with a nucleic acid marker [~~probe~~]sequence comprising at least 20 contiguous nucleic acid bases from a sequence, or its complement, in Chromosome 16 from chromosomal

regions selected from the group consisting of regions P7, P55, P89, P90, P92, P93, P94, P95, P99, P154, and P208.

30. (Amended) The method of claim 29 wherein the marker ~~[probe]~~sequence is selected from the group consisting of Stanford Human Genome Center Marker Probes SHGC-2835, SHGC-9643, SHGC-11302, SHGC-2726, ~~[SHGC-361232]~~SHGC-36123, SHGC-35326, IB391, GATA7B02, SHGC-33727, and SHGC-13574.

33. (Amended) The method of claim 26 wherein the ~~[CT-1]~~nucleic acid sequence copy number in the test sample cells is at least two-fold greater than the copy number of unamplified marker sequences.

35. (Amended) The method of claim 28 wherein the cancerous tissue is selected from the group consisting of breast cancer, prostate cancer, colon cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colorectal cancer, endometrial ~~[canceroma]~~carcinoma, salivary gland carcinoma, kidney cancer, vulval cancer, thyroid cancer, and head and neck carcinoma.

**Clean Set of All Pending Claims****February 27, 2003**

Claims 1, 25, 28-30, 33, and 35 are amended as follows, wherein strikeout in brackets [00] indicates deleted terminology and underling 00 indicates added terminology. An indication of claim amendment is included for convenient reference.

1. (Twice Amended) A method of diagnosing tumor in a mammal, the method comprising:

(a) detecting the level of expression of a nucleic acid sequence in a test sample of tissue cells obtained from the mammal, wherein the cells are suspected of uncontrolled growth and wherein the detecting is by contacting, under high stringency conditions, nucleic acid of the test sample cells with a nucleic acid probe comprising at least 20 contiguous nucleic acid bases from DNA 58125 (SEQ ID NO:1) or its complement (SEQ ID NO:2);

(b) detecting, as in step (a) the level of expression of the nucleic acid sequence in a control sample of tissue cells of the same cell type that do not exhibit uncontrolled growth; and

(c) comparing the expression level of the nucleic acid sequence in the test cells with the expression level in the control cells, wherein a higher expression level in the test sample indicates the presence of tumor in the mammal.

3. The method of claim 1 wherein said test sample is obtained from an individual suspected to have neoplastic cell growth or proliferation.

24. The method of claim 3 wherein the test sample is from a human.

25. (Amended) The method of claim 1 wherein the expression level of the nucleic acid sequence in the test sample cells is at least two-fold greater than in the control cells.

26. The method of claim 1 wherein the test sample is from cancerous tissue.

27. (Amended) The method of claim 26 wherein the cancerous tissue is selected from the group consisting of breast cancer, prostate cancer, colon cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colorectal cancer, endometrial carcinoma, salivary gland carcinoma, kidney cancer, vulval cancer, thyroid cancer, and head and neck carcinoma.
28. (Amended) A method of diagnosing tumor in a mammal, the method comprising:
- (a) detecting the number of copies of nucleic acid sequence in a test sample of tissue cells obtained from the mammal, wherein the cells are suspected of uncontrolled growth and wherein the detecting is by contacting, under high stringency conditions, nucleic acid of the test sample cells with a nucleic acid probe comprising at least 20 contiguous nucleic acid bases from DNA 58125 (SEQ ID NO:1) or its complement (SEQ ID NO:2);
  - (b) detecting the number of copies of a nucleic acid marker sequence on the chromosome encoding the nucleic acid sequence in the test sample, which marker gene is not amplified; and
  - (c) comparing the copy number of the nucleic acid sequence in the test cells with the copy number of the marker sequence, wherein a higher nucleic acid sequence copy number indicates the presence of tumor in the mammal.
29. (Amended) The method of claim 28 wherein the marker sequence is detected by contacting, under high stringency conditions, nucleic acid of the test sample with a nucleic acid marker sequence comprising at least 20 contiguous nucleic acid bases from a sequence, or its complement, in Chromosome 16 from chromosomal regions selected from the group consisting of regions P7, P55, P89, P90, P92, P93, P94, P95, P99, P154, and P208.
30. (Amended) The method of claim 29 wherein the marker sequence is selected from the group consisting of Stanford Human Genome Center Marker Probes SHGC-2835,

SHGC-9643, SHGC-11302, SHGC-2726, SHGC-36123, SHGC-35326, IB391, GATA7B02, SHGC-33727, and SHGC-13574.

31. The method of claim 28 wherein said test sample is obtained from an individual suspected to have neoplastic cell growth or proliferation.
32. The method of claim 31 wherein the test sample is from a human.
33. (Amended) The method of claim 26 wherein the nucleic acid sequence copy number in the test sample cells is at least two-fold greater than the copy number of unamplified marker sequences.
34. The method of claim 28 wherein the test sample is from cancerous tissue.
35. (Amended) The method of claim 28 wherein the cancerous tissue is selected from the group consisting of breast cancer, prostate cancer, colon cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colorectal cancer, endometrial carcinoma, salivary gland carcinoma, kidney cancer, vulval cancer, thyroid cancer, and head and neck carcinoma.